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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/827,024	04/19/2004	K. Keith Kwok	217538	2493

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EXAMINER	
KRISHNAN, GANAPATHY	
ART UNIT	**PAPER NUMBER**
1623	
MAIL DATE	**DELIVERY MODE**
10/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/827,024	KWOK ET AL.	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,17-32 and 38-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15, 17-32 and 38-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 7/16/2007 has been received, entered and carefully considered. The following information provided in the amendment affects the instant application:

1. Claims 16 and 33-37 have been canceled.

2. Claims 1, 15 and 20 have been amended.

3. Remarks drawn to claim objections and rejections under 35 USC 112, second paragraph, 102 and 103.

Claims 1-15, 17-32 and 38-44 are pending in the case.

Claim Objections

The objection regarding the numbering of claims has been overcome by amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of Claim 44 under 35 U.S.C. 112, second paragraph, as being indefinite for recitation of the term complicated has been overcome by applicants providing documentation in support of the said term being definite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of Claims 33 and 35 under 35 U.S.C. 102(b) as being anticipated by Nail et al (J. Pharmaceutical Sciences 2002, 91(4), 1147-55) has been rendered moot by cancellation of the said claims.

Claims 17, 20, 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Nail et al (J. Pharmaceutical Sciences 2002, 91(4), 1147-55; document AI in IDS of July 26, 2004) is being maintained for reasons of record.

Applicants have traversed the rejection by arguing that the Nail reference teaches Tobramycin formulation, wherein the initial solution comprises from 5% to 11% t-butanol (Figures 3-6). The instant claims require that the solution initially comprises about 4.5% by volume or less of t-butanol. Hence Nail does not anticipate the instant claims.

Applicants' arguments are not found to be persuasive.

Applicants have amended the claim to recite that the initial solution (claim 1, step (a)) comprises about 4% by volume or less of t-butanol. The term "about" does not clearly define the percentage of t-butanol. Nails teaching of the initial solution having a 5% t-butanol content is close to about 4.55 as instantly recited and still reads on the instant claims. Nail et al teach a lyophilized formulation of Tobramycin (page 1149, left column, second and third full paragraphs; limitations of claim 17). They also teach compositions that contain less than 1.1% t-butyl alcohol (see figure 4 at page 1152; limitations of claim 20). The lyophilized Tobramycin is dissolved in 2mL of distilled water (page 1149, second full paragraph; limitations of claim 29).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 16 and 36-37 35 U.S.C. 103(a) as being unpatentable over Nail et al (J. Pharmaceutical Sciences 2002, 91(4), 1147-55; document AI in IDS of July 26, 2004), has been rendered moot by cancellation of the said claims.

The rejection of Claims 1-15, 18-19, 21-28, 30-32, 34 and 38-39 under 35 U.S.C. 103(a) as being unpatentable over Nail et al (J. Pharmaceutical Sciences 2002, 91(4), 1147-55; document AI in IDS of July 26, 2004) is being maintained for reasons of record.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Applicants have traversed the rejection by arguing that:

1. Nail teaches that the initial concentration of t-butanol is 5%.

2. Under two sets of conditions used by Nail, the solution having 5% initial concentration of t-butanol gives a higher residual percentage of t-butanol compared to the one that has an initial concentration of 6%.

3. One of skill in the art would therefore start with an initial concentration of t-butanol that is about 6% or more and not less than about 5% based on the teaching of Nail.

Applicants arguments are not found to be persuasive.

Nail et al, drawn to powdered Tobramycin, teach the preparation of freeze-dried Tobramycin (lyophilized) wherein Tobramycin in combination with t-butyl alcohol (abbreviated as TBA by Nail) was freeze dried under vacuum at –45°C for 6 hours. Nail also teaches primary drying at –20°C for 50 hours at 100 mtorr pressure followed by secondary drying at 25°C for ten hours at 100 mtorr (page 1148, right column, see section entitled freeze-drying). According to Nail the freeze dried Tobramycin shows phase separation and does not break apart, retain high levels of the alcohol and do not readily reconstitute (page 1151, left column first paragraph). From this teaching one of ordinary skill in the art would recognize that reducing the amount of t-butyl alcohol is necessary in order to produce a powder that can reconstitute as fast as the single-phase system.

The amount of residual t-butanol obtained under the two sets of conditions for 5% and 6% initla concentration of t-butanol is not significantly different (0.9% vs 0.75%) to dissuade a

skilled artisan to avoid starting with an initial concentration of about 6% or above. Moreover, the initial concentration of t-butanol as instantly recited is also very close to the concentration taught in the prior art.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce a lyophilized formulation of Tobramycin via a method as instantly claimed and also make compositions as instantly claimed since the general process steps and conditions for the same is seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to use a method as instantly claimed since it is seen from the teaching of Nail that removal of residual alcohol is critical. It is also well known in the art that application of vacuum reduces the boiling point of a liquid and facilitates the removal of a solvent without decomposition. Hence slow heating of the Tobramycin containing residual alcohol under vacuum will help remove most of the residual alcohol to produce a single phase Tobramycin that will reconstitute easily. One of ordinary skill in the art will also be motivated to make compositions with different amounts in sealed vials as instantly claimed since such sealed compositions would not absorb moisture and cake.

It is well within the purview of one of ordinary skill in the art to adjust the process parameters like pressure, temperature and rate of heating based on the teaching of nail inorder to get an optimal removal of the residual t-butyl alcohol.

The rejection of Claims 41-44 under 35 U.S.C. 103(a) as being unpatentable over Igarashi (US 4,166,114) in combination with Lagace et al (J. of Liposome Research, 1999, 993), 301-312, is being maintained for reasons of record.

Applicants have traversed the rejection by arguing that the prior art does not teach or suggest a method of treating a disease in a patient using a formulation comprising lyophilized Tobramycin wherein the lyophilized Tobramycin is in the form of a free flowing powder.

Applicants arguments are not found to be persuasive.

Igarashi teaches a method of treating bacterial infections in humans and animals, which include soft tissue infections and urinary tract infections among others via administration of a composition comprising Tobramycin (col. 9, lines 38-46). Igarashi *suggests* the *desirability* of lyophilized *powders* and also suggests preparations in vials in a separate container in unit dosage form for making injectable solutions just before use and also dosages (col. 9, lines 9-37 and lines 46-54). However, Igarashi does not exemplify the said treatment with examples suing lyophilized Tobramycin.

Lagace et al teach the efficacy of Tobramycin against several bacteria including P. aeruginosa, Strenotrophomonas maltophilia, Burkholderia cepacia, E. coli and S. aureus bacterial colonies (abstract; page 305-308-efficacy and killing curves).

Igarashi teaches the use of lyophilized powders. Whether it is free flowing or not is not critical to the method of treatment. This is also known to one of skill in the art.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use lyophilized Tobramycin and its compositions for the treatment of bacterial infections in a patient as instantly claimed since such is seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to do so since Tobramycin is seen to bee efficacious against several bacteria and the use of the lyophilized *powder* also has the

advantage of preserving it for a long period of time and make injectable compositions just before use, as taught by Igarashi.

Conclusion

Claims 1-15, 17-32 and 38-44 are rejected

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GK

9/27/07

Shaojia A. Jiang
Supervisory Patent Examiner
Art Unit 1623